Predisposing genetic differences contribute to vulnerability to escalate cocaine intake in rats

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Aims: Endogenous opioids play a central role in mediating the reinforcing properties of cocaine. The striatum is a key brain region implicated in reward and motivation. Recently we published a new model of cocaine self-administration in which rats are exposed to operant sessions lasting 18 h for 14 days, which models closely the human cocaine exposure (Picetti et al., 2010). Indeed we reported Lewis rats escalated progressively their cocaine consumption while Fischer did not. Therefore, the aim of this study was to investigate if differences in striatal endogenous opioids could contribute to the vulnerability to escalate cocaine intake.

Methods: Adult male Fischer and Lewis rats were trained to self-administer cocaine intravenously. Saline-yoked rats were used as control. Rats were sacrificed 24 h following the last operant session. Striatal cDNA samples ($n = 10–11$/group) were analyzed by qPCR targeting endogenous opioid peptides and receptors.

Results: POMC mRNA expression was lowered significantly by cocaine self-administration in the dorsal striatum of both Fischer and Lewis rats. Further, POMC basal level was significantly lower in Fischer than in Lewis rats. Striatal pDyn gene expression was increased by chronic cocaine in both strains; the increase seen in Lewis was much greater than in Fischer. The basal levels of pDyn mRNA was higher in Fischer than in Lewis rats. Finally, Fischer rats showed a higher basal level of mu opioid receptor mRNA than Lewis rats. Extended cocaine self-administration increased the mu opioid receptor mRNA only in Lewis, but not Fischer rats.

Conclusions: The present results corroborate the hypothesis that predisposing genetic factors could contribute to the escalation of intake in rodent models of cocaine addiction. High basal striatal pDyn could countermodulate the cocaine-induced increase in mu receptor, and decrease the progression from impulsive to compulsive drug use.

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Naltrexone inhibits the subjective effects of salvinorin-A in humans

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Aims: Salvinorin-A is a terpene found in the leaves of the plant Salvia divinorum. When administered to humans, salvinorin-A induces an intense but short-lasting modified state of awareness, sharing features with those induced by the serotonergic psychedelics. However, unlike substances such as psilocybin, or mescaline, salvinorin-A shows affinity in vitro for the kappa-opioid receptor rather than for the serotonin-2A receptor. In the present study we aimed to assess whether the subjective effects induced by salvinorin-A in humans are caused by the drug's interaction with opioid receptors.

Methods: Eight healthy volunteers participated in four experimental sessions. They received the following drug combinations one week apart: placebo/placebo, placebo/salvinorin-A, naltrexone/placebo and naltrexone/salvinorin-A. Naltrexone was administered at a dose of 50 mg orally and salvinorin-A at 1 mg vaporized. Subjective effects were assessed using visual analog scales (VAS), the Hallucinogen Rating Scale (HRS), the Addiction Research Center Inventory (ARCI) and the Altered States of Consciousness questionnaire (APZ).

Results: After the placebo pre-treatment, salvinorin-A induced an intense dream-like state characterized by significant increases in VAS measuring modifications in body perception, perception of time, detachment from external reality and visual imagery. Significant increases were also observed in all subscales of the HRS and APZ and in the LSD subscale of the ARCI. These effects were effectively prevented by naltrexone. Following pre-treatment with this non-specific opioid antagonist, the intensity of subjective effects induced by salvinorin-A was markedly attenuated and scores on the administered instruments were significantly decreased.

Conclusions: These results support opioid receptor agonism as the mechanism of action underlying the subjective effects of salvinorin-A in humans.

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Role of substance abuse in physical and mental health trajectories throughout the deployment cycle: A national guard study

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Aims: Identifying trajectories of health and substance abuse is fundamental to understanding risk for negative health outcomes throughout a military serviceperson's deployment cycle. This study aims to identify sub-groups of National Guard service members who are likely to be more negatively affected by deployment in the context of "citizen soldier's" dual roles.

Methods: Retrospective reports of National Guard service member surveyed approximately 2–4 months post-deployment (over 51% to Afghanistan) ($N = 467$) were collected for one year prior to the most recent deployment, during deployment and at post-deployment. We used a latent growth mixture model using physical and mental health and substance use measures for three time periods to identify underlying trajectory groups. A multinomial mixed model was used to determine whether combat exposure, stress and other factors related to deployment predicted trajectory group membership.

Results: The best fit four-class model identified a low risk group ($n = 260$) (group 1), a high risk for smoking group ($n = 122$) (group 2), a medium risk for mental health problems group ($n = 33$) (group 3) and a high risk for physical and mental health problems group ($n = 52$) (group 4). Significant changes in physical and mental health indicators occurred among groups 3 and 4 during